

“MARKED-UP” COPY SHOWING CHANGES

(Page 6, at line 6)

Figure 2 is a representation of the amino acid consensus sequence (SEQ ID NO 4) from HBV DNA polymerase proteins encompassing regions which are conserved in the RNA polymerase protein. These regions are shown as domains A-E and are underlined. In the consensus sequence the M in the YMDD motif is designated as amino acid number 550. The amino acids which are subject to mutation during 3TC and/or FCV treatment are shown in bold. An asterisk (*) indicates greater than three amino acid possibilities at this position of the consensus sequence. The HBsAg major hydrophilic region containing the neutralisation domain is indicated by a double line and the polymerase mutations which alter the HBsAg are indicated in italics.

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Figure 3 is a representation of the nucleotide sequence from various strains of HBV encoding the surface antigen (SEQ ID NOS 5-16). The amino acid sequence of the surface antigen beginning at amino acid 108 is shown above the nucleotide sequence.

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The preferred surface component of the HBV of the present invention is the HBV surface antigen (HBsAg). It is proposed in accordance with the present invention that the HBsAg of the HBV variants exhibit an altered immune profile relative to an HBsAg from a reference HBV. For the purposes of the present invention, a reference HBV conveniently comprises an HBsAg with an amino acid sequence substantially as set forth by Norder *et al.* (9) which encompasses all known genotypes of HBV (currently A through F). The amino acid sequence of an HBsAg and which is considered to define a reference HBV is set forth below in Formula I (SEQ ID NO 1):

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The present invention extends to any novel mutant or novel use of a mutant of the HBsAg carrying a single or multiple substitution, addition and/or deletion or truncation in the amino acid sequence of HBsAg as compared to the amino acid sequence set forth in Formula I. In an alternative yet related embodiment, the present invention extends to any single or multiple amino acid substitution, addition and/or deletion or truncation in the amino acid sequence of HBsAg relative to the amino acid sequence set forth in Formula I as defined by a single or multiple amino acid substitution, addition and/or deletion to the catalytic region of the HBV DNA polymerase set forth below in Formula II (SEQ ID NO 2):

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The altered HBsAg molecules of the HBV variants of the present invention may also be defined at the nucleotide level. The nucleotide sequence encoding the HBsAg from a reference HBV is set forth below in Formula III (SEQ ID NO 3):